The most reasonable explanation which we have been able to formulate in explanation of the present case has been a vasomotor one, probably engrafted upon some sclerotic change in the bundle or its nutrient vessels. The auriculoventricular bundle is, of course, nourished by definite branches of the coronary artery. Vascular sclerosis is often curiously localized in distribution. Thus, in the field of medicine which we have been considering Karcher and Schaffner found the bundle well preserved in a case of high-grade coronary sclerosis, and Aschoff describes well-marked arterial disease affecting the small arteries which supply the bundle, and yet the bundle itself was in an apparently healthy condition. It is conceivable that if for some reason the blood supply of the bundle was temporarily cut off or diminished, it would cease functionating as long as the anemia kept up, and again take on its normal activity when its blood supply was reëstablished. That there may have been some such diminution of blood supply resulting from round-cell infiltration, arterial spasm, or constriction, or alteration in local blood pressure, would be nearly as difficult to deny as it would be to prove. At all events, this seems to be the most rational explanation which can be offered to explain the case in question.

I wish to express my indebtedness to Drs. Norris, Stengel, Pepper, and Thayer for their assistance in the study of the case.

A CLINICAL STUDY OF TWO CASES OF CARDIAC DEATH.

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Much remains to be determined regarding the causes of cardiac complications arising during the course of, or following, the acute infectious diseases. A great deal of light is being thrown upon this subject by the experimental studies of Pearce,[1] Fisher,[2] Welsh and Flexner,[3] Bolton and Bown,[4] Fleischer and Loeb,[5] and Sharp.[6] Postmortem investigations in the infectious diseases have demonstrated profound changes in the heart muscle, as the result of the action of the various microbiotic poisons. These conditions are analogous with changes occurring in the skeletal muscles in like disorders. The first studies upon the condition of the heart muscle in infections were made in a case of typhoid fever, but the most minute observations have been carried on in regard to diphtheria. In diphtheria, in addition to myocardial changes, there has been demonstrated degeneration of the medullary centres, of the peripheral vagus, and of the cardiac plexus (Vincent and P. Meyer). Romberg and Paessler have pointed out that the circulatory disturbances which arise in animals infected with pneumococcus, Bacillus diphtheriæ, and Bacillus pyocyaneus are caused almost exclusively by central paralysis of the vasomotor apparatus.

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[1] A note on the Production of Vascular Lesions in the Rabbit by Single Injections of Adrenalin, Albany Med. Annals, xxviii, 51.

[2] Ueber Arterienenkrankungen durch Adrenalin Injectionen, Münch. med. Woch., 1905, iii, 928.

[3] Histological Changes in Experimental Diphtheria, Bulletin Johns Hopkins Hospital, 1891; The Histological Changes Produced by the Toxalbumin of Diphtheria, ibid., 1892, iii, 17.

[4] Pathological Changes in Central Nervous System in Experimental Diphtheria, Brain, xxx, 365.

[5] Archives Int. Med., iii, 78.

[6] Jour. Anat. and Phys., 1897, xxxi, 199.

In applying observations made on pneumococcic septicemia in animals to human beings afflicted with pneumonia, it must be remembered that in pneumonia the condition is not quite analogous, since in this an additional strain is thrown on the heart by reason of obstruction in the pulmonary circuit. Krehl[7] concludes his discussion of the subject of cardiac involvement in diphtheria by saying that all that we can state definitely at present regarding the subject, is that the diphtheria poison injures the heart muscle and the vasomotor apparatus. It is probable that in the near future further studies in experimental myocarditis, induced by the injection of adrenalin or by inoculation with toxins, will throw additional light upon the matter.

The interest of this subject lies not alone in the field of the experimental physiologist and of the pathologist. The clinician must add his observations as to the effect which these poisons produce upon the living, as demonstrable at the bedside. The symptoms of cardiac involvement are not infrequently somewhat obscure; yet, if such signs as are present be disregarded, there may occur an unexpected and perhaps an avoidable death, which, by careful examination, could have been at least foreseen.

Case I.—M. J., a female, aged six years, a well-nourished child, with no history of previous severe illness. She was first seen October 5, 1906, when she was found to have typical tonsillar diphtheria. Diphtheria bacilli were subsequently demonstrated in pure culture. On the following day the exudate had spread to the pharynx. There was moderate toxemia. The urine was normal. The heart sounds were markedly clear, and the pulse regular and full. The fever was not at any time high. Antitoxin was administered on this and on the succeeding day—6500 units in all—after which the child began to improve, and by October 10 she was practically well; the exudate had disappeared; the temperature had fallen to normal; the general condition was so good that the parents regarded the little patient as well. As yet there was no circulatory change demonstrable.

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[7] Diseases of the Heart, Nothnagel's Encyclopedia, 635.

On October 11, in the evening, the child complained of feeling chilly, but did not have a true rigor. She had been particularly cheerful all day. The evening was cool; so she was wrapped in a blanket and was soon quite comfortable. On October 12 she had a sudden attack of severe epigastric pain with vomiting; these symptoms continuing throughout the day. There had been no indiscretion in diet and her bowels had been moving freely. A physical examination showed that the heart sounds had become muffled, and it was noticed that the radial pulse was markedly arrhythmic. The child's face was pale and anxious, and the skin surface was decidedly cool. The examination of the abdomen showed epigastric tenderness, but was otherwise negative. The family was warned of the danger, and instructed to keep the patient absolutely quiet upon her back, to have some one person with her constantly, and to avoid all excitement. The use of the bed pan was insisted upon. The further course of the case was as follows:

On October 13 vomiting and pain were still present, but they were of a less severe nature; the pulse was very weak and intermittent; the heart impulse was weak, the muscular sound poor, but no murmur was audible.

On October 14 improvement continued; there was no pain; there was occasional slight vomiting, but nourishment was retained fairly well; the bowels moved; the pulse was of better quality. In the evening the child was left alone for a short time by the member of the family who was acting as nurse. The patient called, and, receiving no answer, became much excited, screamed violently and repeatedly, and, when the nurse returned, was so nervous that "she shook all over," and could not be quieted for a long time.

On October 15, when she was seen about midday the condition was fairly good; she had slept the greater part of the night, the pulse was somewhat better in quality than it had been previously; but the heart sounds were muffled, and the beat irregular as to rhythm and force; no murmur was heard. One hour later I was called hurriedly and found her in collapse. Her nurse, on being questioned, said that at about 12.30 the child had called out that she was about to have a movement of the bowels. The bed pan was brought, but she became greatly excited and insisted on being allowed to sit up. This the nurse (a sister) finally allowed her to do, although she had been fully warned against the danger of such proceeding. Almost immediately the little patient gave a long sigh, her arms dropped to her sides, she became deathly pale, and could return no answer to the frenzied questions put to her. She died at 4.30 P.M., never having reacted nor regained consciousness.

The case appears to be a typical one of cardiac death occurring in convalescence from diphtheria. Only a few points of interest will be considered in regard to it.

Time of Appearance of the Cardiac Symptoms. Two forms exist, an early and a late. Heart failure in the acute stage is seen only in the severest forms of infection. It may occur without warning, or there may be prodromal signs of failure of the circulation. Death in convalescence may be sudden, but is more frequently preceded by signs and symptoms of abnormality of heart action. "But the most curious thing is that, for a long time, weeks after the disease itself has run its course, and when the patient is convalescent there is still danger of the occurrence of severe circulatory disturbances" (Krehl[8]).

Danger Signs. Vomiting is, as a rule, an indication of the beginning of degeneration of the vagus nerve. "There is no one symptom in the convalescent stage of diphtheria which is of so grave import as a sudden unexplained attack of vomiting. Very few patients in this condition recover" (McCollum[9]). Other serious symptoms are marked pallor, coming on perhaps suddenly, and abdominal pain and tenderness. Among the dangerous cardiac symptoms are an increase in frequency, or a marked slowing of the heart beat. Irregularity of force and rhythm, with a muffling of the muscular sounds are always to be taken seriously as of bad prognostic omen. The association of gallop rhythm with late vomiting renders the outlook almost hopeless (White and Smith[10]).

Frequency. Romberg and Schmaltz claim that circulatory disturbances occur in 10 to 20 per cent. of all cases of diphtheria.

Effect of Antitoxin. Authorities diagree. Krehl[11] says that as far as can be judged, serum treatment has no appreciable influence upon the frequency of circulatory disturbances. White and Smith[12] conclude that antitoxin does not affect the heart, unfavorably, but that, on the other hand, its early use prevents the appearance of grave heart complications. Rosenau and Anderson[13] have reported the remarkable prophylactic effect of the early use of antitoxin against postdiphtheritic paralyses in guinea-pigs.

Treatment. When severe heart complications have developed, absolute rest in bed and absolute avoidance of excitement, perhaps for weeks, are necessary. One may, however, be governed somewhat by the stage of the illness and the general condition. If no serious trouble has developed within four weeks the patients are, as a rule, safe from this complication (White and Smith). They are not, however, entirely out of danger.

Action of the Toxins and Microörganisms upon the Circulatory Apparatus. The infection is frequently mixed—a fact which complicates the problem. Baginsky[14] says: "If we ask ourselves what anatomical change the heart muscle in these conditions and processes has suffered we would be greatly mistaken if we assumed that they are always very marked or constantly of the same nature. Occasionally, in fact, nothing is found which could at all explain the loss in the action of the heart; and this is especially the case if death has occurred quite rapidly. In these cases, probably, lesions of the cardiac nerves and ganglia arise which can only be demonstrated with the greatest difficulty. On the other hand, however, there is found, especially in those cases in which the agony has lasted some time, and in which the improved conditions have varied with renewed collapse, the grossest changes in the heart muscle; fatty degeneration of the muscular structure, gross changes in the nuclei of the muscles, and complete fragmentation or hemorrhagic dissemination of the muscular tissue, and with this adhering thrombi which have most probably occurred during life."

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[8] Loc. cit.

[9] Modern Medicine, ii, 416.

[10] Communications of Mass. Med. Soc., 1904. Quoted by McCollum, loc. cit.

[11] Loc. cit., 637.

[12] Loc. cit.

[13] Trans. Assoc. Amer. Phys., xxii, 26.

[14] Mod. Clin. Med., p. 516.

The theory of Eppinger is accepted by Trumpp[15]—that of a separation of the fibrils of the heart muscle from their sheaths—a myolysis from toxic œdema. Adami[16] regards vagus degeneration as the most satisfactory explanation of the sudden deaths which occur in diphtheria. His is a view to which I incline, as best explaining the terrible sequel of this case.

Case II.—Miss P. Y., aged fifty-four years. She had been a healthy child up to her ninth year, at which time she had an attack of scarlet fever, moderate in its severity. There were apparently no complications, and she was subsequently in good health until three years later, when she passed through a severe attack of diphtheria. She was confined to her bed for four months. The cause of this protracted illness is unknown, but the family states definitely that there were no paralyses. A short time after she was able to be on her feet again, she began to suffer from severe attacks of asthma, usually lasting for three or four days. During the intermissions, of several weeks' duration, she was entirely free from respiratory disorder. She never, however, regained her previous bodily strength.

When twenty years of age she began, for the first time, to complain of palpitation during her asthmatic attacks, although she continued free of cardiac symptoms during the intermissions. Following a change of dwelling to a somewhat higher altitude, the attacks of asthma and palpitation greatly diminished as to frequency, and she had comparative freedom for nearly twelve years, when the symptoms of cardiac insufficiency began to return, and to assume the major rôle. She still had attacks of asthma and suffered from bronchitis and emphysema; but the heart was evidently somewhat crippled at this time, for she was very short of breath on exertion, and œdema set in. There were frequent attacks of tachycardia, and the family later began to notice a dusky color about her lips and fingers. Her asthmatic attacks were comparatively infrequent from this time on, but the cyanosis became so marked that a sister described her as having times when her hands would be "black to the knuckles." The latter condition set in about two years before her death, and had no relation with her attacks of dyspnœa. During the last few months there were "two occasions when the forehead and cheeks became almost black." She complained of dyspeptic symptoms and of pain in the right hypochondrium. During the two months before her death, her sister noticed a throbbing of the veins in her neck—this an independent observation and not the result of a leading question. The skin was always sallow. She began to be apathetic, but in spite of her discomfort was able to attend to light duties about the house.

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[15] Diseases of Children, Pfandler and Schlossman, ii, 386.

[16] Principles of Pathology, p. 433.

I was called to see her on March 6, 1909, and found her walking about her room in great respiratory distress. Her face and finger nails were livid, the general surface dusky, and the conjunctivæ icteric. She was troubled with frequent cough, and was expectorating a viscid, blood-stained mucus. Physical examination revealed a general arteriosclerosis, a radial pulse of marked irregularity and weakness, throbbing jugulars (ventricular venous pulse), an apex beat diffuse in the fifth and sixth interspaces somewhat within the nipple line. The transverse area of cardiac dulness extended from three and one-half finger breadths to the right of the sternum, to the left nipple line. The lungs showed evidence of chronic bronchitis. There were also many piping asthmatic rales. There was an area of beginning consolidation at the right base posteriorly. Examination of the heart showed a tumultuous irregular action, the muscle sound very poor—apparently a soft, systolic murmur at the apex and over the lower portion of the sternum. It was difficult to be certain of this, as the conditions for examination were exceedingly unfavorable. There were very poor aortic and pulmonic second sounds. The liver extended to the level of the umbilicus, was tender to the touch; no pulsation could be detected. An extremely unfavorable prognosis was given owing to the patient's age and to the condition of the heart. Her family was warned of the danger of sudden death.

When she was seen next morning the patient's mind was relatively clear. The temperature was 102°. There was little evidence of toxemia. The heart conditions had remained apparently unchanged. The consolidation at the right base had increased in area, and a beginning involvement of left base was apparent. A few hours afterward the very competent nurse in attendance took the patient's pulse and found it unchanged. She stepped into the hall and was absent, she says, but a minute. When she returned she was shocked to see the patient evidently in a dying condition. In a minute or so breathing had ceased.

I will not attempt to discuss this case in detail, but only in relation to the cardiac complication. As the patient was not seen until near the termination of her case, and as any conclusions which are drawn must rest upon the history and upon the untrained observations of members of her family up to the appearance of her terminal pneumonia, a complete diagnosis of her condition was beset with many, perhaps insuperable, difficulties. Further, the presence of her pneumonia and of her excessively weak heart, masked certain symptoms and made perhaps of doubtful import such others, as the enlargement of the liver, the jaundice, the cyanosis, and the increase of cardiac dulness to the right which was present at the time of examination. A point which, from a study of her history, strikes me at the very beginning, is the comparatively late period at which symptoms of a failing circulation began to develop—that is, the amount of work which a weak heart may be able to perform.

That the original cause of weakness of the heart muscle may be traced to the diphtheria forty years before seems not impossible. We have noted that at that time the patient had been confined to her bed for four months. It is stated quite definitely by an intelligent member of the family that there were present no paralyses to account for this long illness. The known frequency of myocardial complications in the disease under consideration makes it, therefore, not unlikely that to a damaged heart muscle must be attached the blame of this protracted convalescence. The duration of the illness corresponds with the course of myocarditis of convalescents, some cases of which are often protracted for weeks, or even months.

The important point to be considered is, whether a myocarditis arising in childhood could affect the heart during so long a period as forty-two years. As bearing upon this point I quote from Krehl:[17] "The restitutio ad integrum in many cases of diphtheritic heart disease that end in recovery is so complete that an ordinary physical examination reveals nothing whatever. But it is a question, nevertheless, whether the heart is really absolutely sound, expecially whether it has the same functional capacity as before, or, in other words, whether its capacity is adequate to the demands incident to the individual's mode of life. The more we study heart diseases the more we are impressed with the extreme complexity of the etiology; an infectious disease that has run its course many years before a definite disease of the heart develops, appears, nevertheless, to be capable of influencing the development of this disease, although the interval between the two events may have been marked by perfect health. Possibly the first disease prepared the soil for the second."

We note that for eight years after her diphtheria the patient had no cardiac symptoms, or, at least, none that were observed. During this time, she was greatly troubled by attacks of asthma, the pre-

[17] Loc. cit., 638.

disposition to which disease may have arisen through catarrhal conditions of the respiratory mucous membrane resulting from her diphtheritic infection. It is possible that the cardiac affection was responsible. The long period of asthma without apparent cardiac inadequacy, and the fact that the asthma diminished as the heart became less and less able to carry on its work, suggest, however, that some exciting cause was present outside of the myocardium. It may be noted as a matter of interest that McPhedran[18] claims that true asthma is very rarely due to diseases of the heart. Jellenk and Cooper[19] suggest that cardiac asthma may arise in certain instances as a right-sided angina. Whether we consider the asthma of cardiac origin or not, it is certainly of interest that, for over a period of many years, circulatory disturbances played only a secondary role in the clinical picture, and that it was not until the later years of her life that symptoms of cardiac incompetence became of overshadowing importance. A longitudinal section of her history shows us, then: a period of eight years of asthma without circulatory disturbances; thirty-two years of asthma with coincident cardiac distress but freedom between attacks; and a later period during which the asthmatic attacks became less frequent while the trouble with the heart increased. We have learned that it was only during the last two years of her life that marked cyanosis became noticeable to the untrained members of her family, but that the marked pulsation of the veins of her neck were visible for two months before her death.

What had happened to the heart during this period? To an organ which we have assumed to have been early weakened by a toxic myocarditis and later to have participated in a general condition of malnutrition, which we have seen existed since her twelfth year, has been added a frequently recurring strain. The cardiac strain in asthma falls particularly upon the right heart, and in the patient under consideration the throbbing veins of the neck and the attacks of extreme cyanosis with subicteric color of the skin and conjunctivæ, noted by the family, give support to the view that during the later period there was a gradually increasing dilatation of the right ventricle with resulting incompetence of the tricuspid valves. The marked congestion of the liver observed at the time of examination and the history of right hypogastric pain give some further support to this view. . . .

Further cause of dilatation of the right heart may have existed in an insufficiency of the mitral valve. Clinical proof of such condition is wanting; but, when we remember how often a muscular insufficiency of the mitral valve exists, even in a pure myocarditis, and when we further consider the frequency with which myocarditis and true endocarditis co-exist, it would certainly have been quite within ordinary experience to have had such cause of pulmonary engorgement present in this case. That no mitral murmur was heard at the time that the patient came under observation could not, of course, exclude such condition.

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[18] Modern Medicine, iii, 712.

[19] Amer. Med. Jour., vol. 1, No. 9.

Finally, a persistent low blood pressure may have been an additional cause of weakness of the heart muscle as a whole. How much, if any, of this was due to vasomotor influences and to a massing of blood in the splanchnics cannot be determined. We can only say that at the beginning of the patient's pneumonia she had a very low arterial pressure, and that it is not unlikely that such a condition had been present for some time. Here, then, we would have a possible establishment of a vicious circle, for, as soon as the left ventricle can no longer maintain a sufficient degree of pressure in the aorta to maintain the requisite pressure in the coronary artery, the myocardium suffers from hyponutrition at the very time when it can least afford to dispense with its proper supply (Hoover[20]).

Then as a last straw comes pneumonia, with a toxin in the circulation capable of further damaging the heart muscle, and an added work is thrown upon the already weakened right ventricle by reason of the obstruction in the pulmonary circuit. That the heart could not respond to this additional call is shown by the weakness of the pulmonic sound throughout.

I have spoken of dilatation of the right ventricle resulting in failure at closure of the tricuspid valves—a relative incompetence which is almost the only form seen developing in adult life, except in connection with previously existing valvular disease involving other valves of the heart. The mechanism of this functional incompetence is, that as the dilating right ventricle expands, the fibrous ring surrounding the auriculoventricular orifice becomes stretched. A larger opening is thus formed, and as the chordæ tendinæ cannot elongate, the cusps can no longer meet in close apposition. Further, "It is a question whether the inability of the muscle to lessen the ventricular cavity to its normal size in systole does not play a large, if not the chief part, for if at the height of systole the cavity were no larger (than normal), it is conceivable that even with a dilated ring no regurgitation might occur; but if with a dilated ventricle the degree to which the ventricle can contract be lessened, then the cavity is fuller at the end of systole than normal, and the valve cusps are not properly approximated" (Osler[21]).

SUMMARY. It may, therefore, be concluded with a fair degree of certainty that the cause of death was incompetence of a heart muscle, probably the seat of a chronic myocarditis. This condition may have originated at the time of the infection with diphtheria during childhood, or, at least, the soil may have been prepared at that time for subsequent cardiac disease. That the scarlatinal infection may have exerted some unfavorable influence cannot, of course, be denied. At any rate, owing to repeated strain and to various unfavorable conditions there gradually developed the incompetence of the muscle for the work required of it. Dilatation of the right ventricle set in, with relative insufficiency of the tricuspid valves; the fatal end was precipitated by a sudden increase in resistance in the pulmonary circuit, with possibly a further weakening of the muscle as a result of the action of the toxic products of a pneumococcic infection.

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[20] Modern Medicine, iv, 31.

[21] Ibid., 240.

It is regretted that autopsies could not be obtained in either of the above cases; but, since the wide field of speculation into which a bedside study of certain heart cases may lead us opens up many subjects which even a careful postmortem examination might fail to make wholly clear, their report seems, nevertheless, justifiable.

INFLUENZAL SEPTICEMIA.

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The invasion of the deep tissues and the blood by the influenza bacillus has been a matter of much doubt, and up to recent times has received but little bacteriological confirmation. That it does more or less frequently invade the blood stream can no longer be doubted. When we consider the accumulating evidence of the comparative frequency among severe influenzal infections, of such complications as endocarditis, arteritis, phlebitis, arthritis, etc., we must be impressed, I think, with the probable frequency with which this organism finds its way into the blood and there succeeds in living and multiplying. Doubtless a simple transmission by the blood to other parts, without the organism actually growing in the blood, may occur.

One striking feature noted in connection with certain cases of the grip is the marked prolongation of the fever, suggesting the continued operation of the organism in the tissues rather than a mere delay in the recovery from an infection lasting only a few days. In many of these prolonged attacks there has been no bacteriological evidence forthcoming to prove what organ formed the nidus of the bacillus. However, in not a few there has been demonstrated a definite complication, such as otitis media, pleurisy, pneumonia, pericarditis meningitis, arthritis, etc., and from these has been isolated the influenza bacillus. There are still other cases of prolonged fever in which none of these complications appear, or at least play a minor